

Remarks

Claims 67-74 have been cancelled, and claims 41-42, 63 and 66 have been amended. Claims 75-81 have been added. Thus, claims 41-42, 56-63, 66 and 75-81 are pending. In compliance with 37 C.F.R. § 1.121(b), Applicants have provided marked-up versions of the amended claims, showing all of the proposed changes.

I. OBJECTIONS

The examiner objects to the Figures 1, 4-6. Applicants submitted with their response of February 3, 2003 formal drawings for the referenced figures. Thus, rejection has been obviated.

II. REJECTIONS UNDER 35 U.S.C. §112, ¶1

The examiner rejects claims 41-42, 56-63 and 66-74 under 35 U.S.C. §112, ¶1 for allegedly lacking written description. Applicants respectfully traverse the rejection.

The invention provides methods of identifying compounds that associate with TACE using atomic coordinates that comprise the coordinates of Table 1, or a substantial part thereof, to design an associating compound that forms a bond with a catalytic domain of a TACE polypeptide. The specification identifies several regions within the TCD that are useful for designing associating compounds. For example, the specification suggests using the atomic coordinates for the S1' or S1'S3' regions to design compounds which associate with a TCD. *See e.g.* Application, page 8, line 21 to page 9, line 4 and page 30, line 26 to page 31, line 7. In addition, since TACE is a zinc endopeptidase, the specification emphasizes the importance of residues which interact with a catalytic zinc. For example, see the specification at page 9, line 10 to page 10, line 21, and at page 24, line 24 to page 25, line 10.

Accordingly, one of ordinary skill in the art would recognize readily that applicants understood, at the time of filing, that associating compounds could be designed using a substantial part of the atomic coordinates of table 1, wherein the substantial part included the S1' region, the S1'S3' pocket or atoms which bind a catalytic zinc. To advance prosecution in the instant case, however, applicants have amended the claims and believe that the rejections have been obviated.

III. REJECTIONS UNDER 35 U.S.C. §112, ¶1

The examiner rejects claims 41-42 under 35 U.S.C. §112, ¶1, alleging that the claims are not enabled by the specification. In effort to expedite prosecution, applicants have amended the instant claims, and assert that the amendments obviate the rejection.

IV. REJECTIONS UNDER 35 U.S.C. §101

The examiner rejects claims 56-63 and 67-74 under 35 U.S.C. §101, for allegedly being directed to non-statutory subject matter. Applicants respectfully traverse the rejection.

The examiner asserts that, "[a]s further research would have to be performed to determine what, if any activity or effect the identified compound would have, the result of the method is not a useful, concrete and tangible one." Office Action dated October 2, 2002, pg. 6, first paragraph. So stating, the examiner has imposed on the applicants a requirement to show the utility of an unclaimed invention and, thereby, committed a legal error.

Applicants are not claiming compounds that associate with TACE. Rather, the present invention is directed to methods of identifying compounds that associate with TACE. Thus, the proper inquiry is whether these methods achieve a useful, concrete and tangible result. As evidenced by the examples and the previously-submitted declaration of Dauphine Barone, the methods achieve their intended purpose. Moreover, by identifying TACE-associating compounds, the invention has revolutionized the process for developing TACE modulators. Therefore, as the claimed methods provide substantial utility to the pharmaceutical arts, the rejection should be withdrawn.

In view of the foregoing remarks it is believed that the application is in condition for allowance. A favorable disposition of the application therefore is solicited.

Respectfully submitted,

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Date

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Marked-up Version of Amended Claims

41. (Amended) The method according to claim [63] 66, wherein said associating compound is an inhibitor, mediator, or other compound that regulates TNF- α -converting enzyme activity.

42. (Amended) The method of claim [63] 66, wherein said associating compound is a competitive inhibitor, un-competitive inhibitor, or non-competitive inhibitor.

63. (Amended) A method of identifying a compound that associates with tumor necrosis factor- α -converting enzyme (TACE), comprising (A) using atomic coordinates that comprise the coordinates of Table 1 **[or a substantial part thereof]** to design an associating compound that forms a bond with a catalytic domain of a TACE polypeptide, and (B) determining via computer-generated models whether said compound associates with said catalytic domain[,

wherein said substantial part comprises atomic coordinates of regions selected from the group consisting of the S1' region, the S1'S3' pocket and atoms which bind a catalytic zinc].

66. (Amended) A method of identifying a compound that associates with tumor necrosis factor- α -converting enzyme (TACE), comprising (A) using atomic coordinates that comprise the coordinates of Table 1 **[or a substantial part thereof]** to design an associating compound that forms a bond with a catalytic domain of a TACE polypeptide, (B) synthesizing said compound, and (C) determining *in vitro* whether said compound associates with said catalytic domain[,

wherein said substantial part comprises atomic coordinates of regions selected from the group consisting of the S1' region, the S1'S3' pocket and atoms which bind a catalytic zinc].